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(51) International Patent Classification ⁷ : C12N 15/12, 5/10, 1/21, A01K 67/027, C12N 15/00, C12Q 1/68, C07K 16/18	A3	(11) International Publication Number: WO 00/22122 (43) International Publication Date: 20 April 2000 (20.04.00)
(21) International Application Number: PCT/IB99/01730 (22) International Filing Date: 12 October 1999 (12.10.99) (30) Priority Data: 60/103,955 13 October 1998 (13.10.98) US 60/106,457 30 October 1998 (30.10.98) US (71) Applicant (for all designated States except US): GENSET [FR/FR]; 24, rue Royale, F-75008 Paris (FR). (72) Inventors; and (75) Inventors/Applicants (for US only): BLUMENFELD, Marta [FR/FR]; 5, rue Tagore, F-75013 Paris (FR). BOUGUEL- ERET, Lydie [FR/FR]; 14, rue Vouillé, F-75015 Paris (FR). CHUMAKOV, Ilya [FR/FR]; 196, rue des Chèvrefeuilles, F-77000 Vaux-le-Penil (FR). COHEN, Daniel [FR/FR]; 1, boulevard Richard Wallace, F-92200 Neuilly-sur-Seine (FR). ESSIUX, Laurent [FR/FR]; 107, rue de Reuilly, F-75012 Paris (FR). (74) Agents: MARTIN, Jean-Jacques et al.; Cabinet Regimbeau, 26, avenue Kléber, F-75116 Paris (FR).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> (88) Date of publication of the international search report: 5 October 2000 (05.10.00)
(54) Title: GENES, PROTEINS AND BIALLELIC MARKERS RELATED TO CENTRAL NERVOUS SYSTEM DISEASE (57) Abstract <p>The invention concerns genes, polymorphisms and polypeptides related to central nervous systems disease. Included are the G713 gene, the G713 protein and G713 biallelic markers, as well as biallelic markers located on the human chromosome 13q31-q33 locus, and the association established between these biallelic markers and schizophrenia. The invention also provides means to determine the predisposition of individuals to schizophrenia as well as means for the diagnosis of this disease and for the prognosis and detection of an eventual treatment response to therapeutic agents acting against schizophrenia.</p>		

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 99/01730

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C12N5/10 C12N1/21 A01K67/027 C12N15/00
C12Q1/68 C07K16/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LI S -H ET AL: "NOVEL TRIPLET REPEAT CONTAINING GENES IN HUMAN BRAIN: CLONING, EXPRESSION, AND LENGTH POLYMORPHISMS" GENOMICS,US,ACADEMIC PRESS, SAN DIEGO, vol. 16, no. 3, 1 June 1993 (1993-06-01), pages 572-579, XP000196589 ISSN: 0888-7543 cited in the application	1,15,45, 46, 50-54, 56,57
Y	the whole document -& EMBL/GENBANK DATABASES Accession no L10374 Sequence reference HSMRNAC 23 June 1993 XP002134451 --- -/--	3,4, 6-14, 16-44, 47,55

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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Date of the actual completion of the international search

10 April 2000

Date of mailing of the international search report

10. 07. 00

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

VAN DER SCHAAL C.A.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 99/01730

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>WANG D G ET AL: "Large-scale identification, mapping, and genotyping of single-nucleotide polymorphisms in the human genome"</p> <p>SCIENCE,US,AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, vol. 280, 1 January 1998 (1998-01-01), pages 1077-1082, XP002089398 ISSN: 0036-8075 the whole document</p> <p style="text-align: center;">---</p>	<p>3,4, 6-14, 16-44, 47,55</p>
Y	<p>KRUGLYAK L: "PASSAGE TEXT. THE USE OF A GENETIC MAP OF BIALLELIC MARKERS IN LINKAGE STUDIES"</p> <p>NATURE GENETICS,US,NEW YORK, NY, vol. 17, no. 1, 1 September 1997 (1997-09-01), pages 22-24, XP002050647 ISSN: 1061-4036 the whole document</p> <p style="text-align: center;">---</p>	<p>3,4, 6-14, 16-25, 28-44, 47,55</p>
Y	<p>WO 98 11222 A (SINAI SCHOOL MEDICINE) 19 March 1998 (1998-03-19) page 17, paragraph 1 page 23, paragraph 3</p> <p style="text-align: center;">---</p>	<p>26,27</p>
Y	<p>DETERA-WADLEIGH S D ET AL: "A high-density genome scan detects evidence for a bipolar-disorder susceptibility locus on 13q32 and other potential loci on 1q32 and 18p11.2."</p> <p>PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 MAY 11) 96 (10) 5604-9., XP002134450 the whole document</p> <p style="text-align: center;">---</p>	<p>42,47</p>
Y	<p>MING-WEI LIN ET AL: "SUGGESTIVE EVIDENCE FOR LINKAGE OF SCHIZOPHRENIA TO MARKERS ON CHROMOSOME 13 IN CAUCASIAN BUT NOT ORIENTAL POPULATIONS"</p> <p>HUMAN GENETICS,DE,BERLIN, vol. 99, no. 3, March 1997 (1997-03), pages 417-420, XP000876937 the whole document</p> <p style="text-align: center;">---</p>	<p>42,47</p>
X	<p>EMBL/GENBANK DATABASES Accession no AA989298 Sequence ID AA989298 27 August 1998 "National Cancer Institute, Cancer Genome Anatomy Project..." XP002135005 the whole document</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	<p>1,45,46</p>

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 99/01730

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>EMBL DATABASE Accession no B75361 Sequence ID B75361 14 Januari 1998 ADAMS M ET AL: "Use of BAC end sequences for sequence-ready map building" XP002135179 the whole document -----</p>	1

INTERNATIONAL SEARCH REPORT

national application No.
PCT/IB 99/01730

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 51-56 could be considered as a mere presentation of information or a computer program, Rule 39.1 (v and vi) PCT, the search has been carried out as far as possible in our systematic documentation.
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1, 3, 4, 6-25, 28-47, 50-57 partially, 26, 27 completely

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/IB 99/01730

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1 3 4 6-25 28-47 50-57 partially 26 27 completely

human G713, (fragments of) nucleotides encoding G713
including biallelic markers derived from these sequences,
antibodies against G713 and their uses

2. Claims: 1 51 53-57 partially 2 completely

(fragments of) nucleotide sequence SEQ ID NO 31 and its use

3. Claims: 1 3 4 6-14 16-25 28-44 47 50-
57 partially 5 48 49 completely

(fragments of) 13q31-q33 biallelic marker containing
sequences SEQ ID NO 32-69 and their uses

4. Claims: 1 15 45 46 51-57 partially

murine homologue of G713, nucleotides encoding it,
antibodies against it and their uses

INTERNATIONAL SEARCH REPORT

International Application No. PCT/IB 99/01730

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 16-18 relate to an extremely large number of possible compoundss. In fact, the claims contain so many options, that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear (and/or concise), namely the polynucleotides mentioned in tabel 2

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

Information on patent family members

PCT/IB 99/01730

Form PCT/ISA/210 (patent family annex) (July 1992)